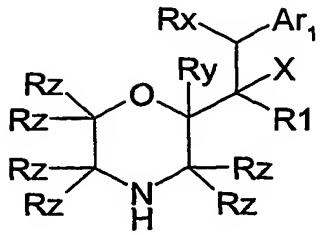
CLAIMS

1. A compound of formula (I)



(I)

wherein,

X is OH, C1-C4 alkoxy, NH_2 or NH(C1-C4 alkyl);

Rx is H or C1-C4 alkyl;

Ry is H or C1-C4 alkyl;

each Rz group is independently H or C1-C4 alkyl, with the proviso that not more than 3 Rz groups may be C1-C4 alkyl;

R1 is C1-C6 alkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkylthio (optionally substituted with 1, 2 or 3 fluorine atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms), C3-C6 cycloalkoxy, C1-C4 alkylsulfonyl, cyano, -CO-O(C1-C2 alkyl), -O-CO-(C1-C2 alkyl) and hydroxy); C2-C6 alkenyl (optionally substituted with 1, 2 or 3 halogen atoms); C3-C6 cycloalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; C4-C7 cycloalkylalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; or CH_2Ar2; and

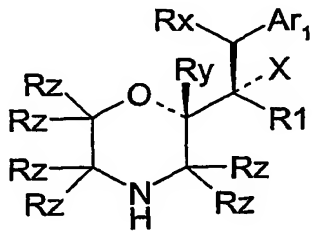
Ar1 and Ar2 are each independently a phenyl ring or a 5- or 6-membered heteroaryl ring each of which is optionally substituted with 1, 2 or 3 substituents (depending upon the number of available substitution positions) each independently selected from C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1,

2 or 3 halogen atoms), -CO-O(C1-C4 alkyl), cyano, -NRR, -CONRR, halo and hydroxy and/or with 1 substituent selected from pyridyl, thiophenyl, phenyl, benzyl and phenoxy each of which is optionally ring-substituted with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), carboxy, nitro, hydroxy, cyano, -NRR, -CONRR, SO_2NRR and SO_2R; and

each R is independently H or C1-C4 alkyl;

or a pharmaceutically acceptable salt thereof.

2. A compound of formula (II)



(II)

wherein, X, Rx, Ry, Rz, R1 and Ar1 are as defined for formula (I) in claim 1; or a pharmaceutically acceptable salt thereof.

3. A compound as claimed in any preceding claim or claim 30 wherein X is OH.

4. A compound as claimed in any preceding claim or claim 30 wherein Rx is H.

5. A compound as claimed in any preceding claim or claim 30 wherein Ry is H.

6. A compound as claimed in any preceding claim or claim 30 wherein each Rz is H.

7. A compound as claimed in any one of claims 1 to 6 or 30 to 32 wherein R1 is C1-C6 alkyl optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkylthio (optionally substituted with 1, 2 or 3 fluorine atoms), C1-

C4 alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms), C3-C6 cycloalkoxy, C1-C4 alkylsulfonyl, cyano, -CO-O(C1-C2 alkyl), -O-CO-(C1-C2 alkyl) and hydroxy.

8. A compound as claimed in any one of claims 1 to 6 or 30 to 32 wherein R1 is C2-C6 alkenyl optionally substituted with 1, 2 or 3 halogen atoms.

9. A compound as claimed in any one of claims 1 to 6 or 30 to 32 wherein R1 is C3-C6 cycloalkyl optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkoxy and hydroxy wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond.

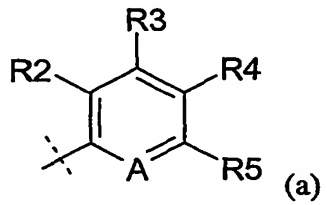
10. A compound as claimed in any one of claims 1 to 6 or 30 to 32 wherein R1 is C4-C7 cycloalkylalkyl optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkoxy and hydroxy wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond.

11. A compound as claimed in any one of claims 1 to 6 or 30 to 32 wherein R1 is CH_2Ar2 wherein Ar2 is a phenyl ring or a 5- or 6-membered heteroaryl ring each of which is optionally substituted with 1, 2 or 3 substituents (depending upon the number of available substitution positions) each independently selected from C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -CO-O(C1-C4 alkyl), cyano, -NRR, -CONRR, halo and hydroxy and/or with 1 substituent selected from pyridyl, thiophenyl, phenyl, benzyl and phenoxy each of which is optionally ring-substituted with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), carboxy, nitro, hydroxy, cyano, -NRR, -CONRR, SO_2NRR and SO_2R.

12. A compound as claimed in any preceding claim or claim 30 wherein Ar1 is a phenyl ring or a 5- or 6-membered heteroaryl ring; each of which is substituted in the

ortho position with a substituent selected from C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -CO-O(C1-C4 alkyl), cyano, -NRR, -CONRR, halo, hydroxy, pyridyl, thiophenyl, phenyl, benzyl and phenoxy, each of which *ortho* substituents is optionally ring-substituted (where a ring is present) with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), carboxy, nitro, hydroxy, cyano, -NRR, -CONRR, SO_2NRR and SO_2R; and each of which is (in addition to *ortho* substitution) optionally further substituted with 1 or 2 substituents each independently selected from C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -CO-O(C1-C4 alkyl), cyano, -NRR, -CONRR, halo and hydroxy.

13. A compound as claimed in any preceding claim or claim 30 wherein Ar1 is a group of the formula (a):



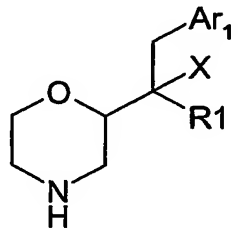
(a)

wherein,

A is N or CR6 (preferably CR6); R2 is C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), halo, hydroxy, pyridyl, thiophenyl, phenyl (optionally substituted with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), or C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms)) or phenoxy (optionally substituted with 1, 2 or 3 halogen atoms); R3 is H; R4 is H; R5 is H, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally

substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), halo or hydroxy; and R6 (if present) is H.

14. A compound of formula (III)



(III)

wherein, X, R1 and Ar1 are as defined for formula (I) in claim1; or a pharmaceutically acceptable salt thereof.

15. A compound according to claim 14 wherein

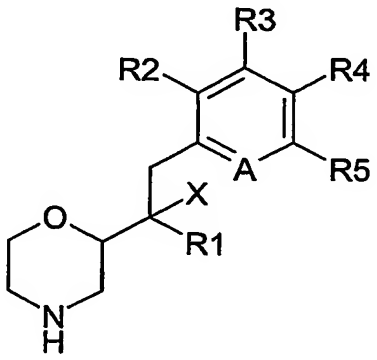
X is OH or NH_2;

R1 is C1-C6 alkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkylthio (optionally substituted with 1, 2 or 3 fluorine atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms), C3-C6 cycloalkoxy, C1-C4 alkylsulfonyl, cyano, -CO-O(C1-C2 alkyl), -O-CO-(C1-C2 alkyl) and hydroxy); C3-C6 cycloalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C, S-C or C=C bond; or CH_2Ar2 wherein Ar2 is a phenyl ring or a pyridyl (preferably 2-pyridyl) ring each of which may be substituted with 1, 2 or 3 substituents each independently selected from C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), halo and hydroxy; and

Ar1 is a phenyl ring or a 5- or 6-membered heteroaryl ring; each of which is substituted in the *ortho* position with a substituent selected from C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -

CO-O(C1-C4 alkyl), cyano, -NRR, -CONRR, halo, hydroxy, pyridyl, thiophenyl, phenyl, benzyl and phenoxy, each of which *ortho* substituents is optionally ring-substituted (where a ring is present) with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), carboxy, nitro, hydroxy, cyano, -NRR, -CONRR, SO_2NRR and SO_2R; and each of which is (in addition to *ortho* substitution) optionally further substituted with 1 or 2 substituents each independently selected from C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), -CO-O(C1-C4 alkyl), cyano, -NRR, -CONRR, halo and hydroxy; or a pharmaceutically acceptable salt thereof.

16. A compound of formula (IV)



(IV)

wherein,

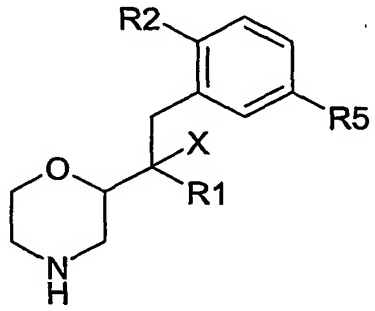
X is OH or NH_2;

R1 is C1-C6 alkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms), cyano, and hydroxy); C3-C6 cycloalkyl (optionally substituted with 1, 2 or 3 halogen atoms and/or with 1 substituent selected from C1-C4 alkoxy and hydroxy) wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C bond; or CH_2Ar2 wherein Ar2 is a phenyl ring optionally substituted with 1, 2 or 3 substituents each independently selected from C1-C4 alkyl (optionally substituted with 1,

2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), halo and hydroxy;

A is N or CR6 (preferably CR6); R2 is C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), halo, hydroxy, pyridyl, thiophenyl, phenyl (optionally substituted with 1, 2 or 3 substituents each independently selected from halogen, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), or C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms)) or phenoxy (optionally substituted with 1, 2 or 3 halogen atoms); R3 is H; R4 is H; R5 is H, C1-C4 alkyl (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), C1-C4 alkylthio (optionally substituted with 1, 2 or 3 halogen atoms), halo or hydroxy; and R6 (if present) is H; or a pharmaceutically acceptable salt thereof.

17. A compound of formula (V)



(V)

wherein,

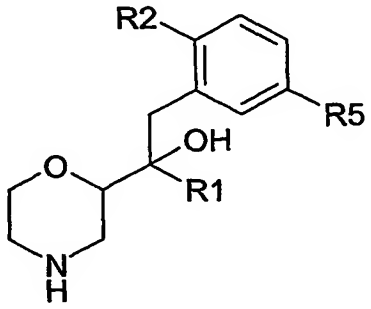
X is OH or NH_2;

R1 is C1-C6 alkyl (optionally substituted with 1, 2 or 3 fluorine atoms), C3-C6 cycloalkyl wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C bond or CH_2Ar2 wherein Ar2 is a phenyl ring optionally substituted with 1 or 2 substituents each independently selected from C1-C4 alkyl (optionally substituted with 1,

2 or 3 halogen atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 halogen atoms), halo and hydroxy;

R2 is C1-C4 alkyl (optionally substituted with 1, 2 or 3 fluorine atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms) or phenyl (optionally substituted with 1, 2 or 3 fluorine atoms); and R5 is H or F; or a pharmaceutically acceptable salt thereof.

18. A compound of formula (VI)



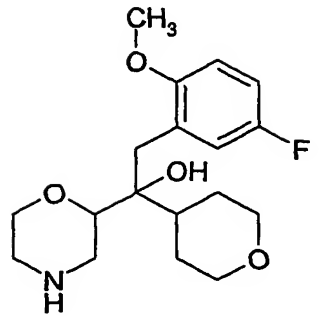
(VI)

wherein,

R1 is C1-C6 alkyl (optionally substituted with 1, 2 or 3 fluorine atoms) or C3-C6 cycloalkyl wherein one C-C bond within the cycloalkyl moiety is optionally substituted by an O-C bond;

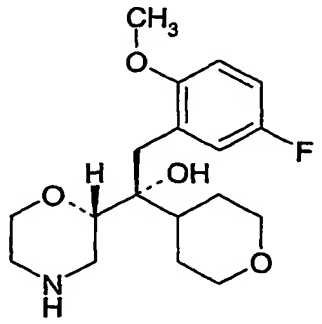
R2 is C1-C4 alkyl (optionally substituted with 1, 2 or 3 fluorine atoms), C1-C4 alkoxy (optionally substituted with 1, 2 or 3 fluorine atoms) or phenyl (optionally substituted with 1, 2 or 3 fluorine atoms); and R5 is H or F; or a pharmaceutically acceptable salt thereof.

19. A compound of the formula



or a pharmaceutically acceptable salt thereof.

20. A compound of the formula



or a pharmaceutically acceptable salt thereof.

21. The hydrochloride salt of a compound according to claim 20 or claim 21.

22. A pharmaceutical composition comprising a compound as claimed in any one of claims 1 to 21, except when dependent upon any one of claims 30 to 32, or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable diluent, excipient or carrier.

23. A compound as claimed in any one of claims 1 to 21, except when dependent upon any one of claims 30 to 32, for use in therapy.

24. A compound as claimed in any one of claims 1 to 21, except when dependent upon any one of claims 30 to 32, or a pharmaceutically acceptable salt thereof for use as an inhibitor of the reuptake of norepinephrine.

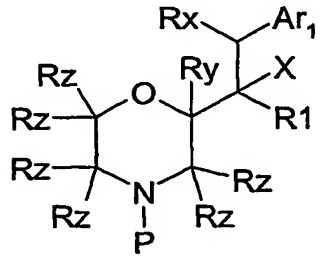
25. A compound as claimed in any one of claims 1 to 21, except when dependent upon any one of claims 30 to 32, or a pharmaceutically acceptable salt thereof for treating disorders associated with norepinephrine dysfunction in mammals.

26. The use of a compound as claimed in any one of claims 1 to 21, except when dependent upon any one of claims 30 to 32, or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of disorders associated with norepinephrine dysfunction in mammals.

27. A method for inhibiting the reuptake of norepinephrine in mammals comprising administering to a patient in need thereof an effective amount of a compound as claimed in any one of claims 1 to 21, except when dependent upon any one of claims 30 to 32, or a pharmaceutically acceptable salt thereof.

28. A method for treating disorders associated with norepinephrine dysfunction in mammals comprising administering to a patient in need thereof an effective amount of a compound as claimed in any one of claims 1 to 21, except when dependent upon any one of claims 30 to 32, or a pharmaceutically acceptable salt thereof.

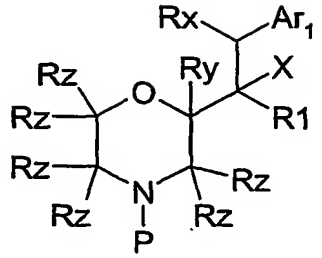
29. A process for the preparation of a compound of formula (I) comprising the step of deprotecting a compound of the formula (XIV)



(XIV)

wherein P represents an N-protecting group and all other variables are as defined for formula (I) in claim 1, to provide a compound of formula (I), optionally followed by the step of forming a pharmaceutically acceptable salt.

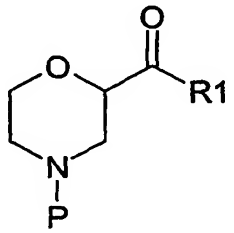
30. A compound of the formula (XIV)



(XIV)

wherein P represents an N-protecting group and all other variables are as defined for formula (I) in claim 1, or a salt thereof.

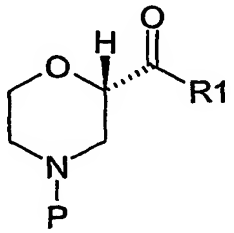
31. A compound of the formula (XIII)



(XIII)

wherein P represents an N-protecting group and all other variables are as defined for formula (I) in claim 1, or a salt thereof.

32. A compound of the formula (XIII)b



(XIII)b

wherein P represents an N-protecting group and all other variables are as defined for formula (I) in claim 1, or a salt thereof.

33. A compound according to any one of claims 30 to 32, or a salt thereof, wherein R1 is a tetrahydro-2H-pyran-4-yl group.

34. A compound according to any one of claims 30 to 33, or a salt thereof, wherein P is a benzyl group.